metes and bounds of the claim indefinite, particularly when said terms are used in reference to chemically modified starting materials and products where the noted terms imply the absence of a complete description of the structural features of said chemically modified starting materials and products" (page 2, line 23 to page 3, line 2 of the Office Action mailed December 31, 2002). Applicant respectfully traverses the rejection.

Applicant respectfully submits that the rejection is not clear. Applicant notes that it is not clear as to which part of the claim the Examiner is applying the rejection, as none of claims 44, 50, and 56 literally recite "chemically modified starting materials and products." In the event that the rejection is maintained, clarification of the rejection is requested in the next Official Communication. To the extent that the Examiner is basing the rejection on use of the terms "comprises" and "comprising" to describe a target polynucleotide, a target RNA, an upstream oligonucleotide, a downstream oligonucleotide, a nucleoside, or an autoligated oligonucleotide product, Applicant respectfully disagrees.

First, Applicant reiterates that the M.P.E.P. clearly indicates that comprising is an accepted transitional phrase (*see, for example* §2111.03, stating that "[t]he transitional term 'comprising', which is synonymous with 'including,' 'containing,' or 'characterized by,' is inclusive or open-ended and does not exclude additional, unrecited elements or method steps"). Applicant respectfully submits that the terms "comprises" and "comprising" are not indefinite, and that claims 44, 50, and 56 particularly point out and distinctly claim the subject matter that Applicant regards as his invention.

Second, Applicant disagrees with the Examiner's assertion that "the noted terms imply the absence of a complete description of the structural features of said chemically modified starting materials and products." Applicant respectfully submits that target polynucleotides, target RNAs, upstream oligonucleotides, downstream oligonucleotides, nucleosides, and autoligated oligonucleotide products are recited in such a manner as to clearly and distinctly convey Applicant's invention to one of skill in the art. For example, the present claims recite a target polynucleotide that comprises a genetic polymorphism (e.g., claim 44, line

3; claim 50, lines 4-5); a target RNA that comprises a genetic polymorphism (e.g., claim 56, line 3); an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group (e.g., claim 44, lines 6-7; claim 50, lines 10-11; and claim 56, lines 6-7); a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group (e.g., claim 44, lines 8-9; claim 50, lines 12-13; and claim 56, lines 8-9); an autoligated oligonucleotide product comprising a universal oligonucleotide probe and a mutant poymorphism probe (e.g., claim 44, lines 15-16; and claim 56, lines 15-16); and an autoligated oligonucleotide product comprising a universal oligonucleotide probe and either a mutant polymorphism oligonucleotide probe or a wild-type polymorphism oligonucleotide probe (e.g., claim 50, lines 26-28). Applicant respectfully submits that the present claims describe structural features of target polynucleotides, target RNAs, upstream oligonucleotides, downstream oligonucleotides, and autoligated oligonucleotide products (e.g., claims 44, 50, and 56) in sufficient detail to clearly and distinctly convey Applicant's invention to one of skill in the art.

Finally, the specification clearly describes the presently recited target polynucleotides (e.g., page 15, line 10 to page 16, line 17), target RNAs (e.g., page 15, line 10 to page 16, line 17), upstream oligonucleotides (e.g., page 11, lines 11-20; page 12, line 14 to page 13, line 14; and page 14, line 11 to page 15, line 8), downstream oligonucleotides (e.g., page 11, lines 11-20; and page 13, line 15 to page 15, line 8), nucleosides (e.g., page 14, line 16 to page 15, line 8), and autoligated oligonucleotide products (e.g., page 16, line 19 to page 17, line 9; and page 23, line 1 to page 25, line 7). Although not required, the specification additionally provides working examples (e.g., pages 25-61).

Moreover, the Examiner stated that "[c]laims 50-54 would be allowable if the limitation of 'less than 7 nucleotides' were also added to the newly added 'wild-type polymorphism oligonucleotide probe' at lines 6-8 of claim 50." Since claims 50-54 also recite the term "comprising," it is unclear whether the Examiner considered these claims to be definite or indefinite. In the event that the next Official Communication is not a Notice of Allowance, clarification of the rejection is respectfully requested in the next Official Communication.

Based on the remarks presented herein above, Applicant respectfully requests that the rejection under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

Rejections under 35 U.S.C. §102(b)

The Examiner rejected claims 44-48, 50-54, and 56-60 under 35 U.S.C. §102(b) as being anticipated by Northwestern University (WO 96/35699). The Examiner also alleged that U.S. Pat. No. 5,681,943 (Letsinger et al.; "AC") and Gryaznov et al., *Nucleic Acids Research*, 22:2366-2369 (1994) ("AW") each include anticipatory subject matter. Applicant respectfully traverses the rejection.

"[F]or anticipation under 35 U.S.C. 102, the reference must teach ***every aspect*** of the claimed invention either explicitly or impliedly." M.P.E.P. §706.02 (emphasis added). Applicant respectfully submits that none of the cited art teaches every aspect of the claimed invention.

In the Amendment and Response mailed on October 23, 2002, Applicant described aspects of the present claims that are ***not taught*** by the above-cited documents (e.g., pages 8-9). This description is incorporated in this Response by reference. However, the Examiner apparently ignored many of the described aspects, and instead chose to focus only on the language recited in the preamble of claims 44, 50, and 56 (i.e., "[a] method for detecting a genetic polymorphism"). Applicant reiterates that for anticipation under 35 U.S.C. §102, a document must teach ***every aspect*** of the claimed invention. Applicant respectfully submits the following examples of ***aspects*** of claims 44, 50, and 56 that are ***not taught*** by any of the cited documents.

For example, the body of claim 44 recites that "when both probes are bound to the target polynucleotide, an end of the universal oligonucleotide probe ***is not directly adjacent*** to an end of the mutant polymorphism oligonucleotide probe" (emphasis added). Further, the body of claim 50 recites "a mutant polymorphism oligonucleotide probe ***of less than 7 nucleotides in length***, a wild-type polymorphism oligonucleotide probe and a universal oligonucleotide probe"

(emphasis added). Finally, claim 56 recites "a method for detecting a genetic polymorphism in a ***target RNA***" (emphasis added). Applicant respectfully submits that the Examiner lacks the discretion to ignore the above-recited claim language.

Applicant respectfully requests that the rejection under 35 U.S.C. §102(b) be reconsidered and withdrawn.

Request for Telephonic Interview with the Examiner and the Supervisory Patent Examiner

In the event that a Notice of Allowance is not immediately forthcoming, Applicant respectfully requests that a telephonic interview be granted between the Examiner, the Supervisory Patent Examiner, and Applicant's Representative, Victoria A. Sandberg, to discuss patentability of the pending claims. Applicant's Representative will contact the Examiner to schedule a telephonic interview.

Amendment and Response
Serial No.: 09/483,337
Confirmation No.: 8254
Filed: January 14, 2000
For: COMPOSITIONS AND METHODS FOR NONENZYMATIC LIGATION OF OLIGONUCLEOTIDES AND DETECTION OF GENETIC POLYMORPHISMS

Summary

It is respectfully submitted that all the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicant's Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
Eric T. Kool

By
Mueting, Raasch & Gebhardt, P.A.
P.O. Box 581415
Minneapolis, MN 55458-1415
Phone: (612) 305-1220
Facsimile: (612) 305-1228
Customer Number 26813

26813
PATENT TRADEMARK OFFICE

Jun 2, 2003
Date

By: _____
Loren D. Albin
Reg. No. 37,763
Direct Dial (612)305-1225

CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that this paper is being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Assistant Commissioner for Patents, Mail Stop RCE, Washington, D.C. 20231, on this 2 day of June, 2003, at 2:15pm (Central Time).

By: _____
Name: SARA E. OLSIN

APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.:09/483,337
Docket No.: 220.00040101

For convenience, all pending claims are shown below.

44. A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and the other oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target polynucleotide, an end of the universal oligonucleotide probe is not directly adjacent to an end of the mutant polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and

detecting the presence of the autoligated oligonucleotide product.

45. The method of claim 44 wherein at least one of the mutant polymorphism oligonucleotide probe and the universal oligonucleotide probe further comprises a detectable label.

46. The method of claim 45 wherein the detectable label is a radiolabel.

47. The method of claim 44 wherein the genetic polymorphism is selected from the group consisting of a single base mutation, a plurality of single base mutations, a deletion, an insertion, and a genetic rearrangement.

48. The method of claim 44 wherein the nucleotide position of the genetic polymorphism is not the nucleotide position corresponding to the ligation junction end of the mutant polymorphism probe.

50. A method for detecting a genetic polymorphism in a target polynucleotide comprising:

providing a mutant polymorphism oligonucleotide probe of less than 7 nucleotides in length that is complementary to a region on the target polynucleotide that comprises the genetic polymorphism;

providing a wild-type polymorphism oligonucleotide probe that is complementary to a region on an analogous wild-type polynucleotide that is analogous to the region comprising the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target polynucleotide at a region that is conserved in the analogous wild-type polynucleotide;

wherein either (i) the universal oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and both polymorphism oligonucleotide probes constitute downstream oligonucleotides comprising, as their 3' ends, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate; or (ii) both polymorphism oligonucleotide probes constitute upstream oligonucleotides comprising, as their 5' ends, a nucleoside comprising a 5' leaving group and the universal oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when a universal probe and a polymorphism probe are bound to the target polynucleotide, an end of the universal oligonucleotide probe is substantially adjacent to an end of the polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target polynucleotide with the universal oligonucleotide probe, the wild-type polymorphism oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and either the mutant polymorphism oligonucleotide probe or the wild-type polymorphism oligonucleotide probe; and

detecting the presence of the autoligated oligonucleotide product.

51. The method of claim 50 wherein at least one of the mutant polymorphism oligonucleotide probe and the universal oligonucleotide probe further comprises a detectable label.

52. The method of claim 51 wherein the detectable label is a radiolabel.

53. The method of claim 50 wherein the genetic polymorphism is selected from the group consisting of a single base mutation, a plurality of single base mutations, a deletion, an insertion, and a genetic rearrangement.

54. The method of claim 50 wherein the nucleotide position of the genetic polymorphism is not the nucleotide position corresponding to the ligation junction end of the mutant polymorphism probe.

56. A method for detecting a genetic polymorphism in a target RNA comprising:

providing a mutant polymorphism oligonucleotide probe that is complementary to a region on the target RNA that comprises the genetic polymorphism;

providing a universal oligonucleotide probe capable of binding to the target RNA at a region that is conserved in the analogous wild-type RNA;

wherein one oligonucleotide probe constitutes an upstream oligonucleotide comprising, as its 5' end, a nucleoside comprising a 5' leaving group and the other

oligonucleotide probe constitutes a downstream oligonucleotide comprising, as its 3' end, a nucleoside comprising a 3' functional group selected from the group consisting of a 3' phosphorothioate, a 3' phosphoroselenoate and a 3' phosphorotelluroate, such that, when both probes are bound to the target RNA, an end of the universal oligonucleotide probe is substantially adjacent to an end of the mutant polymorphism oligonucleotide probe so as to position the 5' leaving group and the 3' functional group in close proximity to one another;

contacting the target RNA with the universal oligonucleotide probe and the mutant polymorphism oligonucleotide probe to yield an autoligated oligonucleotide product comprising the universal oligonucleotide probe and the mutant polymorphism probe; and

detecting the presence of the autoligated oligonucleotide product.

57. The method of claims 56 wherein at least one of the mutant polymorphism oligonucleotide probe and the universal oligonucleotide probe further comprises a detectable label.

58. The method of claim 57 wherein the detectable label is a radiolabel.

59. The method of claim 56 wherein the genetic polymorphism is selected from the group consisting of a single base mutation, a plurality of single base mutations, a deletion, an insertion, and a genetic rearrangement.

60. The method of claim 56 wherein the nucleotide position is not the nucleotide position corresponding to the ligation junction end of the mutant polymorphism probe.